

## Complete Summary

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### GUIDELINE TITLE

Viral hepatitis.

### BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Viral hepatitis. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2005 Oct 7 [Various].

### GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Finnish Medical Society Duodecim. Viral hepatitis. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd; 2004 Dec 7 [Various].

## COMPLETE SUMMARY CONTENT

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## SCOPE

### DISEASE/CONDITION(S)

Viral hepatitis, including:

- Hepatitis A virus (HAV)
- Hepatitis B virus (HBV)
- Hepatitis C virus (HCV)
- Delta agent (Hepatitis D) (HDV)
- Hepatitis E virus (HEV)
- Other viral hepatitises

## GUIDELINE CATEGORY

Diagnosis  
Management  
Prevention  
Treatment

## CLINICAL SPECIALTY

Family Practice  
Infectious Diseases  
Internal Medicine  
Pediatrics  
Preventive Medicine

## INTENDED USERS

Health Care Providers  
Physicians  
Public Health Departments

## GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collect, summarize, and update the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

## TARGET POPULATION

Patients with or at risk for viral hepatitis

## INTERVENTIONS AND PRACTICES CONSIDERED

### Diagnosis

1. Evaluate clinical picture
2. Laboratory tests
  - Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) (hepatitis A, hepatitis B, hepatitis C)
  - Serum immunoglobulin M (IgM) antibodies (hepatitis A, hepatitis B, hepatitis E)
  - Serum immunoglobulin A (IgA) antibodies (hepatitis A)
  - Serum immunoglobulin G (IgG) antibodies (hepatitis E)
  - Hepatitis B e antigen (HBeAg) (hepatitis B)
  - Serum hepatitis C antibodies and ribonucleic acid (RNA) (HCV RNA) (hepatitis C)
  - Serum antibodies against hepatitis D virus (HDV) and HDV antigen (hepatitis D)
3. Liver biopsy (chronic hepatitis)

### Prevention

## General

1. Food and water hygiene
2. Precautions in risk occupations and sexual relationships

## Hepatitis A

1. Avoidance of susceptible foods in high-risk countries
2. Gamma globulin
3. Vaccination

## Hepatitis B

1. Avoidance of high-risk behaviour and blood contact
2. Vaccination of risk groups
3. Post-exposure prophylaxis with anti-hepatitis B immunoglobulin
4. Cleaning wound after exposure to infectious blood

## Hepatitis C

1. Avoidance of intravenous drug use, tattooing, unprotected sexual intercourse

## Treatment/Management

### Hepatitis A

1. Weekly monitoring of serum ALT concentrations
2. Hospital referral, as necessary

### Hepatitis B

1. Determine hepatitis B surface antigen (HBsAg) and hepatitis B core antibodies from suspected source and exposed person
2. Hepatitis B immunoglobulin and vaccine
3. Weekly monitoring of serum ALT concentrations

### Acute Hepatitis

1. Antihistamines or cholestyramine for pruritus
2. Assess serum albumin and prothrombin time
3. Avoidance of all drugs metabolized in the liver
4. Diet with plenty of energy and carbohydrates

### Acute Fulminant Hepatitis (A, B, or C)

1. Interferon alpha and ribavirin
2. Intensive care
3. Liver transplantation

### Chronic Hepatitis C

1. Interferon alpha
2. Pegylated interferon and ribavirin
3. Liver transplantation

Note: Guideline developers considered but did specifically offer recommendations regarding treatment of hepatitis D with interferon alpha.

## MAJOR OUTCOMES CONSIDERED

- Efficacy of prophylaxis
- Efficacy of treatment
  - Virologic remission
  - Viral clearance
  - Transaminase levels and liver histology
- Adverse events related to prophylaxis/treatment

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)  
 Hand-searches of Published Literature (Secondary Sources)  
 Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

### NUMBER OF SOURCE DOCUMENTS

Not stated

### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

#### Levels of Evidence

- A. Strong research-based evidence. Multiple relevant, high-quality scientific studies with homogenic results.
- B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
- C. Limited research-based evidence. At least one adequate scientific study.
- D. No research-based evidence. Expert panel evaluation of other information.

## METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses  
Systematic Review

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

## COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

# RECOMMENDATIONS

## MAJOR RECOMMENDATIONS

The levels of evidence [A-D] supporting the recommendations are defined at the end of the "Major Recommendations" field.

### Basic Rules

- Hepatitis A and E can be best prevented by adequate food and drinking water hygiene, particularly in high-risk countries.
- Hepatitis B and C can be prevented by exercising due care in high risk occupations and in sexual behaviour. The single most important risk factor for hepatitis C is intravenous (IV) drug abuse.
- Prophylaxis against hepatitis A by vaccination is indicated before travelling to high-risk countries.
- Hepatitis B vaccination is indicated in high-risk occupations and for risk groups.
- (Note: Vaccination recommendations in this article are based on Finnish guidelines.)

## Basic Rules of Diagnosis

- If acute viral hepatitis is suspected, the following tests should be performed: immunoglobulin M (IgM) antibodies to hepatitis A virus (anti-HAV IgM), hepatitis B surface antigen (HBsAg), IgM antibodies to hepatitis B core antigen (anti-HBc IgM), and hepatitis C virus (HCV) antibody test.
- If clinically mild hepatitis is associated with symptoms suggestive of mononucleosis (fever, lymphadenopathy, splenomegaly, upper respiratory symptoms) the following additional tests are indicated: mononucleosis rapid test or Epstein-Barr virus (EBV) antibody test and cytomegalovirus (CMV) antibody test.

## Hepatitis A

### Incubation Period

- 15 to 50 days

### Route of Infection

- Usually faecal-oral route

### Clinical Picture

- Acute onset
- Loss of appetite and nausea are the initial symptoms.
- Fever
- Jaundice

### Laboratory Tests

- Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are increased.
- A specific diagnosis can be made by determining serum anti-HAV IgM.
- Total antibodies can be determined to assess the need for prophylaxis. A positive test for total antibodies (and a negative result for IgM antibodies) is indicative of an earlier infection that protects against the disease.
- See Figure 1 in the original guideline document.

### Prophylaxis

- Avoidance of susceptible foods (especially mussels and other seafood) when travelling in high-risk countries
- Short-term, 80% protection may be provided by an injection of gamma globulin (suitable for short journeys lasting less than 1 or 2 months. The dose is 2 mL intramuscularly (i.m.) for adults and 0.02–0.04 mL/kg for children.
- Those who stay a long time in, or travel frequently to, high-risk countries should be vaccinated.
  - For children aged 15 or over and for adults, two doses (Havrix® 1440 ELISA-U/mL, 1 mL) of vaccine are given at months 0 and 6 to 12

- For children aged 1 to 15 years, half the adult dose (0.5mL) is given similarly in two doses at months 0 and 6 to 12
- The dose of Epaxal® vaccine is given the same for adults and children over 2 years of age.
- Hepatitis A+B combination vaccine
  - Given in three doses at months 0, 1, and 6
  - A separate vaccine is available for children below 16 years of age.
- Hepatitis A prophylaxis is always recommended for tourists travelling to the tropics and to the African and Middle Eastern coasts of the Mediterranean. For the Baltic countries, Russia, and former Eastern European countries, prophylaxis is recommended if the intended stay is of a long duration or repeated visits are anticipated.

### Contagiousness

- One week after the onset of jaundice the virus is no longer excreted in the faeces.
- No permanent carrier status has been identified.

### Course of the Disease and Follow-up

- The disease is self-limiting, and no specific treatment is available.
- Serum ALT concentrations should be monitored weekly until they start to decline.

### Hepatitis B

#### Incubation Period

- 1 to 6 months

#### Route of Infection

- Parenteral (syringes used in IV drug use, blood products)
- Sexual contact
- Perinatal transmission

#### Clinical Picture

- Similar to that in hepatitis A, but the onset is often slower
- Joint symptoms in 10 to 20% of patients
- Skin symptoms
- Liver transaminase concentrations rise more slowly than in hepatitis A

#### Laboratory Diagnosis

- Increased serum ALT and AST
- A specific diagnosis is made by determining serum HBsAg and anti-HBc IgM.
- For assessment of infectiousness, the presence of hepatitis B e-antigen (HBeAg) should be determined. (If the result is positive, the patient is likely

- to have active hepatitis and the disease is much more infectious as the virus is actively replicating.)
- See Table 1 below and Figure 2 in the original guideline document.

Table 1. Interpretation of Hepatitis B Serology						
	HBsAg	HbsAb	HBc-IgG	HBc-IgM	HBeAg	HBeAb
Non-infected	-	-	-			
Vaccinated	-	+	-			
Natural immunity	-	+ <sup>1</sup>	+			+
Acute infection						
• early	+ <sup>2</sup>	-	-	-	+/-	
• late	+	-	+	+++	+	
Carrier						
• infective	+	-	+	+/- <sup>3</sup>	+	-
• less infective	+	-	+	-	-	+

1. Negative in about 10-15% of infected persons with a past history of an infection. In such cases, anti-HBc is the only marker of past infection.
2. The first test to become positive (even before clinical symptoms)
3. In the exacerbation of a chronic infection, anti-HBc-IgM may turn positive.

HBsAb -- hepatitis B surface antibody; HBc-IgG -- hepatitis B core-immunoglobulin G; HBc-IgM -- hepatitis B core-immunoglobulin M; HBeAb -- hepatitis Be antibody; HBcAg -- hepatitis B core antigen

### Prophylaxis

- Avoidance of high-risk behaviour (unprotected sex with potential virus carriers, use of unclean injection needles)
- Avoidance of blood contact in occupations that involve contact with human blood

### Vaccination of Risk Groups

- Target groups
  - Neonates with parents who are HBsAg positive (Andre & Zuckerman, 1994; DARE-940807, 1999) [B]. If the mother is a carrier the child should also be given, before the first vaccination, a dose of anti-hepatitis B immunoglobulin (125 IU).
  - Persons living with HBsAg carriers or with patients with an acute hepatitis B infection
  - Sexual partners of HBsAg carriers and sexual partners of patients with an acute hepatitis B infection
  - People with a bleeding disorder requiring regular treatment with blood products



- IV drug abusers, their regular sexual partners, and others living in the same household. It is particularly important to vaccinate newborn babies of mothers who use illicit IV drugs.
- Persons involved in prostitution
- After needle stick injuries and blood exposure when, according to a risk assessment, prophylaxis is required and the case cannot be referred to the occupational health care
- Health workers planning to work in endemic areas
- Vaccination against hepatitis B may also be considered in individual cases for persons who, due to their work, are at an increased risk of blood contact. Vaccination may also be considered for those under the care of such a person. For example:
  - Midwives, dental surgeons, and certain laboratory personnel
  - Staff working at a dialysis unit treating a patient who is a HBs Ag carrier. Other patients of such a unit
  - Staff at a child care centre caring for a child who is an HBsAg carrier. Other children of such a centre
  - Anyone involved in the care of IV drug abusers
- Administration of the vaccine
  - Hepatitis B vaccine 1.0 mL i.m. (0.5 mL for children)
  - The dose is repeated at 1 and 6 months. No booster injections are usually necessary after a successful initial vaccination.
  - About 10% of the vaccinated persons do not obtain sufficient immunity. If the risk of exposure to the virus is high and long-lasting, the presence of immunity should be confirmed serologically about 2 months after the third injection. If there is no antibody response, the risk of exposure should be decreased by, for example, job re-arrangements

#### Immune Prophylaxis After Exposure to the Virus

- Hepatitis B immunoglobulin (HepBQuin®) should be given to neonates of HBsAg positive mothers (+ HBV vaccinations) (Andre & Zuckerman, 1994; DARE-940807, 1999) [B].

#### Action After Exposure to Infectious Blood

- For detailed instructions, see Finnish Medical Society Duodecim guideline "Occupational Exposure to Viral Agents."

#### Contagiousness

- Most patients with hepatitis B infection recover; however, a small proportion (<5%) of adult patients remain carriers of the virus (in the Nordic countries).
- The determination of HBeAg is helpful in the assessment of infectivity.

#### Course of the Acute Disease and Follow-up

- Most cases are self-limiting.
- In the active stage of the disease serum ALT, prothrombin time and, if necessary, prealbumin and bilirubin concentrations are monitored weekly until they start to return to normal.

- HBsAg should be determined 3 months after disease onset.

#### Chronic Stage of the Disease

- If the HBs Ag test remains positive 6 months after the disease onset, the patient is likely to have become a hepatitis B carrier. The carrier status is confirmed by a positive HBsAg test at 12 months.
- The risk of hepatoma is increased in chronic carriers of hepatitis B.

#### Hepatitis C

- The most common type of hepatitis in most countries
- Most cases of non-A-non-B hepatitis after transfusion have been caused by hepatitis C. There are about 500 million carriers of hepatitis C.

#### Incubation Period

- 20 to 120 days

#### Route of Infection

- Parenteral as in hepatitis B but the infectivity is much lower. Sources of exposure include IV drug abuse, tattooing, blood transfusion, and unprotected sex with a hepatitis C positive partner. However, the chance of contracting the virus through unprotected sex is fairly low, and safe sex is not considered absolutely necessary in long-term relationships
- Hepatitis C was a common cause of transfusion hepatitis before the introduction of screening of blood products for hepatitis C virus.
- There are patients who contract hepatitis C without having ever received blood transfusions or belonging to any of the risk groups.

#### Clinical Picture

- The clinical presentation is usually mild. Only about 25% of infected individuals develop jaundice, compared with 50% of those infected with hepatitis B. The disease is often asymptomatic.
- Extrahepatic manifestations such as essential cryoglobulinaemia, glomerulonephritis, autoimmune thyroiditis, Sjögren's syndrome, and porphyria cutanea tarda have been reported in patients with chronic hepatitis C

#### Laboratory Diagnosis

- Fluctuating hepatic transaminase (ALT) concentrations are often the only manifestation of hepatitis C. The concentrations may periodically return to normal.
- Serum ALT and AST concentrations rarely exceed 800 U/L.
- A specific diagnosis is obtained by determining serum hepatitis C antibodies and by ribonucleic acid (RNA) (hepatitis c virus [HCV-]RNA)
  - Antibodies can be detected only after 4 to 6 months from exposure, and after 2 to 4 months from the onset of symptoms.

- HCV RNA is usually positive from at symptom onset.

#### Contagiousness

- The majority of patients with antibodies are carriers of the virus and may spread the infection.

#### Course of the Disease and Follow-up

- Alcohol predisposes the patient to complications of hepatitis C
- The acute phase is often milder than in hepatitis B but the disease becomes chronic more often (in 50-80% of patients).
- Transaminase assays are not helpful in the acute phase because they tend to fluctuate. Monitoring is, however, important if specialist consultation is anticipated.
- The average times from primary infection to liver disease are: chronic hepatitis 13 years, active hepatitis 18 years, cirrhosis 21 years, and hepatoma 28 years. Some patients (20 to 30%) develop cirrhosis of the liver as soon as 5 to 7.5 years after contracting the disease.

#### Delta Agent (Hepatitis D)

- Occurs as a superinfection with hepatitis B
- Caused by a satellite virus that can only infect a HBsAg positive person (both viruses can be acquired at the same exposure)
- Usually IV drug abusers and in HBV carriers
- The course of the disease can be fulminant.
- A specific diagnosis can be made by determining serum antibodies against hepatitis D virus (HDV) (and HDV antigen)
- Treatment with interferon alpha has been tried (Malaguarnera et al., "A meta-analysis," 1996; DARE-961376, 1999) [B].

#### Hepatitis E

- A disease resembling hepatitis A that occurs mainly in developing countries
- A specific diagnosis can be made by determining serum IgG and IgM antibodies to hepatitis E virus (anti-HEV IgG and anti-HEV IgM).
- Hepatitis E should be suspected in patients who have recently visited a developing country, and are likely to have contracted the disease by an oral route, but who have no antibodies against hepatitis A.
- During pregnancy hepatitis E may be fulminant and resultant maternal mortality up to 20%
- Treatment and follow-up are carried out as in hepatitis A.

#### Other Forms of Viral Hepatitis

- Some cases of hepatitis remain without an aetiological diagnosis. It is therefore possible that hepatitis viruses other than those described above do exist

- Up to 90% of patients with mononucleosis induced by Epstein-Barr or cytomegalovirus develop hepatitis. The disease is usually mild, and only about 5% of the patients develop jaundice

### Treatment of Hepatitis and Indications for Specialist Intervention

#### Acute Hepatitis

- The severity is assessed by determining serum albumin and prothrombin time (international normalized ratio [INR] is not suitable). The disease is mild if prothrombin time is over 40% and serum albumin above 30g/L.
- Pruritus can be treated by antihistamines or cholestyramine (4 g/day).
- All drugs that are metabolized in the liver should be avoided.
- The diet should contain plenty of energy and carbohydrates.

#### Acute Fulminant Hepatitis (A, B or C)

- Deep jaundice, cerebral symptoms, progressing liver damage
- Intensive care is indicated. Liver transplantation may be life-saving.

#### Chronic Hepatitis C

- Serum ALT remains elevated 6 months after symptom onset; however, a normal ALT does not rule out the possibility of chronic hepatitis.
- Information on the genotype of the virus is an important guide for treatment decisions. Treatment is more effective for genotypes 2 and 3 than for genotypes 1 and 4.
- Patients with a positive HCV-RNA test, and permanently elevated ALT, more probably have mild chronic hepatitis, and treatment decisions can be made without liver biopsy in genotypes 2 and 3.
- Liver biopsy is indicated in patients with a positive HCV-RNA test and normal ALT, and with genotypes 1 and 4, before considering therapy. Signs of chronic hepatitis in the biopsy are an indication for treatment.
- Treatment consists of a combination of interferon alpha or pegylated interferon alpha (Zeuzem et al., 2000; Heathcote et al., 2000) [A] and ribavirin (Kjaergard et al., 2002) [A] for 48 weeks in genotypes 1 and 4, and for 24 weeks in genotypes 2 and 3.
  - In genotypes 1 and 4 the treatment is discontinued if there is no response at 12 weeks (HCV-RNA still positive).
- With the combination therapy, the virus is eradicated from the blood in about half of the patients.
- Contraindications to the antiviral therapy are decompensated cirrhosis, severe liver dysfunction, cytopenia, immunosuppressive state, human immunodeficiency virus (HIV) positivity, drug or alcohol abuse, severe depression, autoimmune disease, severe generalized disease, and pregnancy.
- Due to the teratogenic effect of ribavirin, reliable birth control should be employed for 6 months after treatment. The same applies to partners of male patients receiving the treatment.
- Liver transplantation is indicated when life expectancy is about 6 months.

### Ability to Work

- In the acute phase, sickness leave is allocated according to normal principles (i.e., the patient may return to work as soon as his/her general condition allows).
- Chronic carrier state should not prevent the person from working.

#### Related Evidence

- Long-acting peginterferon alfa-2a was more effective than interferon alfa-2a in inducing and sustaining virological remission in chronic hepatitis C (Zeuzem et al., 2000; Heathcote et al., 2000).

#### Definitions:

##### Levels of Evidence

- Strong research-based evidence. Multiple relevant, high-quality scientific studies with homogenic results.
- Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
- Limited research-based evidence. At least one adequate scientific study.
- No research-based evidence. Expert panel evaluation of other information.

#### CLINICAL ALGORITHM(S)

None provided

### EVIDENCE SUPPORTING THE RECOMMENDATIONS

#### REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

#### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

### BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

#### POTENTIAL BENEFITS

Accurate diagnosis, effective prophylaxis, and appropriate treatment of viral hepatitis

#### POTENTIAL HARMS

- The teratogenic effect of ribavirin calls for reliable birth control for 6 months after treatment.
- Serious side effects can occur with pegylated interferon and pegylated interferon plus ribavirin.
- Combination therapy with alpha interferon and ribavirin significantly increases the risk of treatment discontinuation and several types of adverse events.

## CONTRAINDICATIONS

### CONTRAINDICATIONS

Contraindications to antiviral therapy include decompensated cirrhosis, severe liver dysfunction, cytopenia, immunosuppressive state, human immunodeficiency virus (HIV) positivity, drug or alcohol abuse, severe depression, autoimmune disease, severe generalized disease, and pregnancy.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better  
Living with Illness  
Staying Healthy

### IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Viral hepatitis. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2005 Oct 7 [Various].

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2004 Dec 7 (revised 2005 Oct 7)

#### GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

#### SOURCE(S) OF FUNDING

Finnish Medical Society Duodecim

#### GUIDELINE COMMITTEE

Editorial Team of EBM Guidelines

#### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: Maija Lappalainen; Martti Färkkilä

#### FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

#### GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Finnish Medical Society Duodecim. Viral hepatitis. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd; 2004 Dec 7 [Various].

#### GUIDELINE AVAILABILITY

This guideline is included in a CD-ROM titled "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: [info@ebm-guidelines.com](mailto:info@ebm-guidelines.com); Web site: [www.ebm-guidelines.com](http://www.ebm-guidelines.com).

#### AVAILABILITY OF COMPANION DOCUMENTS

None available

#### PATIENT RESOURCES

None available

#### NGC STATUS

This NGC summary was completed by ECRI on September 2, 2005. This NGC summary was updated by ECRI on November 8, 2005.

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